Remarks

In the Office Action, the Examiner has rejected claims 1, 4-6, 8,9, 12 and 13 under 35 U.S.C. §103(a) as unpatentable over U. S. Patent 5,941, 867 to Kao in view of U.S. Patent No. 6,070,575 to Gonda. The applicants note that there are no 35 U.S.C. §102 rejections upon any of the claims, as filed. In the office action the examiner has rejected claims 14-22 as being indefinite under 35 USC 112. The Examiner has rejected claims 1, 2, 4, 5, 8, 9, 12-18, 20-24, 27-33, 35-51 and 66-69 under the judicially created doctrine of obviousness-type double patenting over U.S. Patent No. 6,644,309 in view of three other references.

Applicants have amended claim 1 and 14 to include the limitation "manually actuated" to the respiratory medicament delivery device to further define what is regarded as the applicants' invention. Claims 52-65 have been withdrawn per the election filed in Paper number 10. Claim 14 has also been amended to address antecedent basis for the term "cylindrical passage" by deletion of the term "cylindrical" since claim 17, as filed, depends from claim 14, incorporates a limitation of cylindrical passages.

Furthermore, it is noted that the present invention is relates to a manually actuated cartridge for use in medicament delivery devices for the delivery of medicament to a patient. Thus, in certain applications, it might be desirable for a patient to have the ability to actuate a respiratory delivery device without the use of expensive and complex integrated actuation mechanisms or for the use of external devices to actuate the device. An optimal device, in this respect, would be designed to operate at the forces and/or pressures that the human hand is able to exert. Unfortunately, prior art devices can be cumbersome and unwieldy due to the fact that an additional actuation mechanism is required, usually in the form of an electromechanically operable device. Additionally, it would be desirable to have a system which is not permanently integrated and fixed such that various diluents, reconstitution fluids, drugs, dosages, and actuators may be interchanged at he time of administration.

Generally, the present invention is directed to a cartridge for a medicament respiratory delivery device having a body with opposed ends, a passage extending through the body and through the opposed ends. A medicament is stored in the passage. A burstable or pierceable membrane covers and seals the passage at the opposed ends of the body, allowing for selective access to the medicament. The present invention allows a fluid (usually in the form of a gas) to entrain a medicament (usually in the form of a powder) via a manual actuation by enabling the activation of the device at the low forces/pressure applicable by the human hand. Medicament cartridges of the invention employing such low burst pressure films allow for use of simple, manually actuated, pressurization mechanisms such as a syringe or bladder, as described in the specification. Prototype testing indicates that the burstable membranes at the opposite ends of the cartridge in the delivery devices of the present invention rupture nearly simultaneously using only a modest pressure, which falls within the range able to be generated by human hands.

Claim Rejections under 35 USC 112

In the office action the examiner has rejected claims 14-22 as being indefinite for failing to particularly point out and distinctly claim the subject matter, which the applicant regards as the invention. Applicants have amended claim 14 to properly introduce the limitation "passage" by the deletion of "cylindrical" from the subsequent mention of "passage" to clarify antecedent basis and submit that this fully addressed the rejection.

Claim Rejections under 35 USC 103

In the Office Action, the Examiner has rejected claims 1, 4-6, 8, 9, 12 and 13 under 35 U.S.C. §103(a) as unpatentable over U.S. Patent 5,941,867 to Kao in view of U.S. Patent No. 6,070,575 to Gonda. Applicants respectfully traverse that rejection.

Kao is directed to devices and methods for the preparation of pharmaceutical solutions by remote control from a remote location (Column 2, lines 42-45; Column 3,

Lines 52-61). In particular, the invention of Kao is intended for use in low and micro gravity environments. The device utilizes unit dose holders 42 to contain individual pharmaceutical dosages. With reference to Figures 6-8 in Kao, the unit dose holders 42 each include three components: a pressurized gas container 100, a central medicament container 106, and a discharge container 116. As shown in Figure 6, each of the components is initially separate and sealed and filled with a gas, a liquid and a powder, respectively. In addition, as shown in Figure 7, the central container 106 holds a concentrated medicinal solution 107, as a liquid, whereas, the discharge container 116 holds medicinal powder 117 (Column 6, lines 16-23).

Upon applying sufficient force to the gas container 100, enough pressure must be generated in the gas container 100 to rupture a total of five barriers:

(1) membrane 104,

(2) membrane 112 between gas container 100 and central container 106;

(3) membrane 112,

(4) membrane 120 between central container 106 and discharge container 116; and

(5) weakened line of plastic 118, which seals discharge container 116.

In order to achieve the higher pressure required to operate the system of Kao, the device of Kao uses the automatic rupture robotic apparatus of Kao (Column 6, lines 1-3). The device of Kao is controlled without manual processing (Column 6, lines 36-38), which specifically disclaims a manually operable system. Therefore, Kao has no concern for barrier rupture pressures, since Kao is able to rupture the barriers via a robotic apparatus, which is presumed to be able generate high forces and pressures to burst the five barriers in total of the Kao device. Furthermore, as acknowledged by the examiner, there is no disclosure in Kao that indicates or suggests the desirability of a low-pressure burstable barrier. In contrast, the applicant's invention has only two barriers, which are selected such that the burst pressures and forces fall within the range able to be generated by human hands. Additionally, the applicant's invention does not rely on the presence of a liquid (as medicinal solution 107 in Kao) to rupture the barriers, and is able to burst the barriers on the cartridge of the present invention utilizing gas pressure only. Therefore, the disclosure of Kao does not suggest the desirability of a manually actuatable system,

and the fact that the references of Kao and Gonda can be combined is not sufficient to establish *prima facie* obviousness (per MPEP 2143.01).

Furthermore, the device described in Gonda is a container wherein one at least one surface that is collapsible, and the medicament is forced through pores on a portion of the container to be aerosolized. It should also be noted that the portion of the specification relied on by the examiner as a teaching of burst pressures (Col 12, lines 51-56) is actually the container integrity pressure (40 bar or less). In Gonda 40-50 ATM is the maximum pressure the container must withstand without bursting, so that the medicament may be forced from the pores (low resistance filter and then a nozzle) at this pressure without rupturing the container. In addition, Gonda reiterates the fact that the device does not burst at pressures in Col 6, lines 48-52 reproduced below for the examiner's convenience:

> *"The membrane preferably has sufficient structural integrity so that it is maintained in tact (will not rupture) when subjected to force in the amount of up to about 40 bar, preferably up to about 50 bar while the formulation is forced through the pores".*

Gonda repeats the 40-50 bar pressure minimum burst pressure for the filter at Col 7, lines 26-30. Therefore, the 40-50 bar (ATM) pressure postulated by Gonda is not a membrane actuation burst pressure but a package integrity pressure.

With respect to membrane actuation burst pressures, Gonda does postulate that the pores may be "*incompletely formed so that, upon administration of pressure to the entrance side of the film, the exit aperture is formed by bursting outward the exit side of the pores...*" (Col 3 Lines 56-62) and further in (Col 15 Lines 7-20), **nowhere in Gonda is a reference to the pressure at which the bursting is to occur**. Furthermore, the actuation device of Gonda is an electromechanical cam actuated driver as shown in Figure 9. As in Kao, Gonda does not disclose or suggest pressures, which are achievable by manual actuation, since the method of actuation is an electromechanical actuation. Therefore, even if the combination of Kao and Gonda was proper, Gonda does not disclose or suggest membrane actuation burst pressures. In contrast, the applicants'

invention is a manually actuated respiratory medicament delivery device having burstable polyolefin membranes having a burst pressure less than 10 atmospheres.

Furthermore, contrary to the Examiner's assertion that concentrated medicinal solution 107 in Kao is a powdered medicament when, in fact, the powdered medicament 117 is stored in discharge container 116. Thus, the central medicament container 106 in Kao holds a reconstitution liquid 107, which upon activation mixes with powdered medicament 117 contained in discharge container 116. Therefore, the device of Kao does not teach or suggest placing a powdered medicament between two burstable membranes with burst pressures of 10 ATM. A unit dose holder 42 is disclosed by Kao and depicted in FIGS. 6-8, which is believed by the Examiner to teach every limitation of applicants' invention except for a polyolefin burstable membrane having a burst pressure less than 10 ATM and relies on Gonda to overcome this deficiency.

Neither Kao nor Gonda disclose or suggest manual actuation and therefore do not teach the lower burstable membrane having a burst pressure, which is manually achievable. Both Kao and Gonda rely on mechanical actuators to achieve burst pressures, which burst the various membranes at higher pressures than could be achieved manually. In the case of Kao, a total of five membranes are burst. In the case of Gonda, a 40-50 bar (ATM) package integrity pressure is suggested and no burst pressure is suggested.

Thus, in view of the foregoing, the combination of Kao and Gonda, even if proper, does not teach a manually actuated respiratory medicament delivery device having burstable polyolefin membranes having a burst pressure less than 10 atmospheres. Therefore, Applicants' request allowance of claims 1, 4-6, 8,9, 12 and 13. Claim 1, as now amended, is patentably distinct over Kao and Gonda, since it includes the limitation of a manually actuated respiratory delivery device. The combination of Kao and Gonda does not teach or suggest this limitation.

Double Patenting Rejection

In the Office Action, the Examiner has rejected claims 1, 2, 4, 5, 8, 12, 13, 23-24, 35-40, 42, 43 and 66-69 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11, 16, 17, 20 and 26-32 of U.S. Patent No. 6,644,309. The examiner has also rejected claims 1, 9, 27-33, 41, and 44-51 under the

judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-14 and 21 of U.S. Patent No. 6,644,309 in view of claim 21 of U.S. Patent No. 6,443,152 to Lockhart et al. The examiner has also rejected claims 14-18 and 20-22 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11,16,17,20 and 26-28 of U.S. Patent No. 6,644,309 in view of claim 21 of U.S. Patent No. 6,070,575 to Gonda. In response thereto, applicant attaches hereto a Terminal Disclaimer signed by the Agent of record for U.S. Patent 6,644,309. Applicants respectfully submit that such Terminal Disclaimer obviates the obviousness-type double patenting rejections.

New Claims

New claims 72-83 further define aspects of the invention, which are fully supported by the instant specification, *e.g.*, *see* the specification at page 8, paragraph 13, and Fig. 2. Accordingly, no new matter has been added. New independent claim 72 recites a cartridge for a respiratory medicament delivery device having a powdered medicament stored in said passage in the body and burstable polyolefin membranes having a burst pressure less than 10 atmospheres covering and sealing said passage at said opposed ends of said body. As stated previously, Kao does not teach or suggest this combination or criteria for selecting this combination. Without discussing each in detail, it will be appreciated that the claims depending from Claim 72 recite additional features that are not taught or suggested by the prior art.

Conclusion

In view of the Disclaimer filed herein and the Remarks above, applicant respectfully submits that Claims 1-51 and 66-83 are in condition for allowance, and respectfully requests that the Examiner earnestly reconsider his rejections of the present application. Applicant hereby authorizes the Commissioner to charge the fees necessary in connection with this Response and Terminal Disclaimer (Assumed to be $110.00) and any other fees necessary in connection with this application, to Deposit Account Number 02-1666.

In light of the above amendments and remarks, Applicant respectfully requests that the Examiner enter the amendments and consider the remarks made herein. Consideration and prompt allowance of the claims are respectfully submitted.

Any questions concerning this application or amendment may be directed to the undersigned agent of applicant.

Respectfully submitted,

By: _____

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